November 11, 2003

Randy Deskin, Ph.D., DABT
Director, Toxicology & Product Regulatory
Compliance Department
5 Garret Mountain Plaza
West Peterson, NJ 07424

Dear Dr. Deskin:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 6-tert-butyl-3-(chloromethyl)-2,4-xylenol posted on the ChemRTK HPV Challenge Program Web site on July 8, 2003. I commend Cytec Industries, Inc. for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Cytec advise the Agency, within 60 days of this posting on the Web site, of any modifications to their submission. Please send any electronic revisions or comments to the following addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
6-tert-Butyl-3-(chloromethyl)-2,4-xylenol

Summary of EPA Comments

The sponsor, Cytec Industries Inc., submitted a test plan and robust summaries to EPA for 6-tert-butyl-3-(chloromethyl)-2,4-xylenol dated June 4, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on July 8, 2003. The sponsored chemical is 6-tert-butyl-3-(chloromethyl)-2,4-xylenol (CAS No. 23500-79-0).

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The physicochemical data and test plan presented by the submitter are adequate for the purposes of the HPV Challenge Program.

2. Environmental Fate. The submitter needs to provide hydrolysis data for this chemical following OECD guidelines.

3. Health Effects. (a) EPA agrees that the submitter has adequately supported the "closed system intermediate" claim for the substance and is eligible for reduced testing. (b) Adequate data are available for acute toxicity and bacterial mutagenicity assays for the purposes of the HPV Challenge Program. (c) EPA agrees with the submitter's proposal to test for *in vitro* chromosomal aberrations and developmental toxicity; however, the proposed repeated-dose test is not necessary. (d) As an alternative to the developmental toxicity test proposed, per HPV Challenge Program guidance EPA recommends a combined screening test.

4. Ecological Effects. EPA agrees with the submitter's test proposal for ecotoxicity.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the 6-tert-butyl-3-(Chloromethyl)-2,4-xylenol Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The melting point, boiling point, and partition coefficient data provided by the submitter are adequate for the purposes of the HPV Challenge Program. The submitter's plan to test for vapor pressure and water solubility following OECD Guidelines 104 and 105, respectively, is adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation and fugacity are adequate for the purposes of the HPV Challenge Program. The submitter's plan to test for biodegradation following OECD Guideline 301 B or 301 D is adequate for the purposes of the HPV Challenge Program.

Stability in water. In the test plan, the submitter indicates that this chemical is not expected to hydrolyze readily under neutral, ambient conditions. However, EPA notes that 6-tert-butyl-3-(chloromethyl)-2,4-

xylenol contains a benzyl chloride group. Benzyl chloride undergoes hydrolysis with half-lives ranging from 19.1 to 0.58 days in the temperature range of 0.1 to 25 °C. Therefore, the submitter needs to provide hydrolysis data for this chemical following OECD guidelines.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for acute toxicity and bacterial mutagenicity assays for the purposes of the HPV Challenge Program. EPA agrees with the submitter's proposal to test for *in vitro* chromosomal aberrations and developmental toxicity; the proposed repeated-dose test is not necessary.

Repeated-dose Toxicity. Although the submitter proposed testing for this endpoint, no testing is needed because the submitter has provided adequate evidence that 6-tert-butyl-3-(chloromethyl)-2,4-xylenol is a closed-system intermediate.

Reproductive Toxicity. No data were submitted for this endpoint and no testing is proposed because of the submitter's assertion that 6-tert-butyl-3-(chloromethyl)-2,4-xylenol is a closed-system intermediate.

The Guidance for Testing Closed System Intermediates for the Challenge Program at http://www.epa.gov/chemrtk/guidocs.htm allows for a reduced testing protocol provided certain criteria are met. The information required to judge a "closed system intermediate" claim must address the following:

I. Site information
    A. Number of sites.
    B. Basis for "closed process" conclusion at each site.
        1) Process description.
        2) Monitoring data showing no detection.
        3) In the absence of monitoring data, the basis for believing that releases do not occur.
    C. Data on "presence in distributed products."
II. Information on transport (mode, volume, controls, etc)
III. A data search showing that the chemical is not present in other end products.

Closed System Intermediate Review.

EPA believes that information provided by the submitter is adequate to meet the criteria for claiming 6-tert-butyl-3-(chloromethyl)-2,4-xylenol as a closed-system intermediate.

I. Site information

A. Number of sites.

According to the test plan, the subject chemical is manufactured and converted at a single plant site owned and operated by the submitter of the test plan, Cytec Industries, Inc. The Inventory Updates for 1990, 1994, and 1998 list one site, no site, and one site, respectively, as reporting for this chemical.

B. Basis for "closed process" conclusion at each site.

1) Process description.

The subject chemical is manufactured in a closed stainless steel reactor. The manufacturing area is kept under negative pressure relative to non-regulated areas and off-gases are vented through a caustic scrubber. Because a byproduct contaminant is a carcinogen regulated by OSHA, stringent controls applied to prevent exposure to the carcinogen also prevent exposure to the subject chemical, according to

the submission. Following dehydration, the subject chemical is transferred through a closed line to a closed storage tank. The subject chemical is subsequently transferred from the storage tank by a closed line to a closed reactor where it is converted to a commercial chemical product.

Although certain details are lacking, it appears that the subject chemical is manufactured and processed in closed vessels to minimize losses and to preclude exposure to a carcinogenic byproduct.

2) Monitoring data showing no detection.

No workplace monitoring data are available for the subject chemical. The volatility of the subject chemical is characterized as low by the submitter, 12 hPa at 20^{o}C.

C. Data on "presence in distributed products."

The test plan states that the commercial product produced from the subject chemical is analyzed for the subject reactant. The subject chemical is not present at the limit of detection, 0.02% by weight.

II. Information on transport (mode, volume, controls, etc)

The test plan states that the chemical is not transported from the site identified in the test plan.

Developmental toxicity. The submitter plans to conduct a developmental toxicity test (OECD TG 414). However, HPV Challenge Program guidance recommends that a combined screening test (OECD TG 421or TG 422) be used.

Ecological Effects (fish, invertebrates, and algae)

EPA agrees with the submitter's proposed acute tests for fish, daphnia, and algae following OECD Test Guidelines 201, 202, and 203.

Specific Comments on the Robust Summaries

Health Effects

In the acute toxicity robust summary (Ref. 1), the first test substance entry, "as prescribed by 1.1 - 1.4", is in error and can be left blank because test substance information is provided later in the summary. In the second sentence of the second paragraph of the result section, the word "prostate" should be "prostrate."

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.